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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/732,047	12/07/2000	Edwin F. Ullman	BEH-7385	9672

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EXAMINER
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VENCI, DAVID J

ART UNIT	PAPER NUMBER
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1641

DATE MAILED: 02/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>		<b>Applicant(s)</b>	
	09/732,047		ULLMAN ET AL.	
	<b>Examiner</b>		<b>Art Unit</b>	
	David J. Venci		1641	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on December 2, 2005.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-6 and 37-46 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-6 and 37-46 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

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### DETAILED ACTION

Examiner acknowledges Applicants' reply, filed December 2, 2005, which amended claims 1 and 44-46.

Currently, claims 1-6 and 37-46 are under examination.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

### *Specification*

The amendment filed December 2, 2005, is objected to under 35 U.S.C. 132(a) because it introduces new matter into the disclosure. Section 132(a) of 35 U.S.C. states that no amendment shall introduce new matter into the disclosure of the invention. Applicants are required to cancel the new matter in the reply to this Office Action. The added material which is not supported by the original disclosure is as follows:

Amendment to the paragraph bridging pages 3 and 4:

Addition of a "linker attaching the substrate to the product"

Amendment to the paragraph on page 4, lines 20-30:

Addition of a "linker joining the substrate and the detectable product"

Addition of a "product to which the substrate is bound"

Amendment to the paragraph on page 5, lines 1-14:

Addition of an embodiment wherein a "linker may be used to attach a detectable product to a substrate"

Concomitant addition of the term "comprises" and deletion of the term "having"

Amendment to the paragraph on page 5, lines 15-21:

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Addition of an embodiment wherein a "two hapten precursors can be attached to the substrate" (emphasis added)

Amendment to the paragraph bridging pages 5 and 6:

Concomitant addition of the term "comprises" and deletion of the term "via"

Amendment to the paragraph on page 9, lines 5-22:

Addition of a "product that was attached to the substrate by the oxidant cleavable linker"

The amendment filed December 2, 2005, is further objected to because of the following informalities:

Amendment to the paragraph on page 4, lines 20-30:

The recitation of the phrase "binding of a target molecule or analyte to produce a sandwich such as described above" is indefinite. Examiner is unable to locate such a "binding of a target molecule or analyte to produce a sandwich such as described above" in the specification, as amended or originally filed.

Amendment to the paragraph on page 5, lines 1-14:

The mechanism by which "release of the substrate with formation of a first binding site may be accompanied by unmasking of at least some of a second binding site" is mechanistically unclear.

The disclosure is objected to because of the following informalities:

On p. 4, line 14, the recitation of "the specific binding reagents" lacks antecedent basis.

On p. 4, line 14, the recitation of "the sandwich assay" is indefinite. The identity of the one or more sandwiches referenced by "the sandwich assay" is not clear.

On p. 4, lines 16-17, the recitation of "at least one binding site must be created in the product that was not present in the substrate" is indefinite in view of Applicants' amendment filed December 2, 2005, which references a linker joining a substrate and a product.

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On p. 4, lines 18-19, the recitation of "substrates that are convertible to a detectable product" is indefinite in view of Applicants' amendment filed December 2, 2005, which references a linker joining a substrate and a product.

On p. 4, lines 22-23, the recitation of "both the substrate molecules" is indefinite because the identity of "both" substrate molecules is not clear. The specification fails to identify two specific substrates.

On p. 5, line 11, the recitation of "release of the substrate" appears contradictory in view of p. 5, lines 12-13, which recites "[t]his embodiment of the invention does not require separation of the product from the substrate". The object(s) of reference from which the substrate is released is/are not clear.

On p. 9, line 15, the recitation of the phrase "the oxidant cleavable linker" lacks antecedent basis in view of Applicants' amendment filed December 2, 2005, which deletes the anteceding phrase "via oxidant cleavable linker".

The specification is objected to as failing to provide proper antecedent basis for a "digoxigenin-linked biotin linked to the substrate through a reactive oxygen cleavable linker" as recited in amended claim 44. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o).

Appropriate correction, including syntactic and semantic correspondence throughout the specification, is required.

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***Claim Rejections - 35 USC § 112 – first paragraph***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-6 and 37-46 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Specifically, Examiner is unable to locate antecedent support in the specification, as originally filed, for the following claim limitations:

In claim 1:

A substrate that "comprises a detectable product"

A substrate that "comprises a detectable product linked to the substrate"

A substrate that "comprises a detectable product linked to the substrate through a reactive oxygen cleavable linker"

A method comprising any of the preceding.

In claim 44:

A "substrate comprising digoxigenin-linked biotin linked to the substrate through a reactive oxygen cleavable linker".

***Claim Rejections - 35 USC § 112 – second paragraph***

Claims 1-6 and 37-46 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claims 1 and 44, the recitation of the term "substrate" is indefinite because Applicants' specification appears to use the term "substrate" interchangeably with "product" and "surface." For example, Applicants describe a "substrate" that is associated with, and releasable from, a "support" (see p. 5, lines 11, "release of the substrate"). However, Applicants also describe a "product" that is associated with, and releasable from, a "support" and a "substrate" (see p. 5, lines 13-14, "the invention does not require separation of the product from the substrate").

In claim 1, the recitation of the term "sbp" lacks antecedent basis.

In claim 1, the recitation of the pronoun "which" (i.e. "capable of binding specifically to a specific binding pair member or to a complex of two or more sbp members which is capable of binding to the detectable product") (emphasis added) is indefinite. The identity of the object(s) referenced by "which" is not clear.

In claim 44, the recitation of the phrase "said substrate comprising digoxigenin-linked biotin linked to the substrate through a reactive oxygen cleavable linker" lacks antecedent support in the specification and is indefinite. Whether said "substrate" comprises said "reactive oxygen cleavable linker" is not clear.

In claim 44, the recitation of the phrase "releases digoxigenin-linked biotin from the support" lacks antecedent associative relationship between "digoxigenin-linked biotin" and "support."

Claim 44 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. Specifically, the

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preamble of claim 44 does not correspond to the outcome of claim 44. The preamble of claim 44 recites a method for "amplifying a signal", while the outcome of claim 44 results in "detecting the released digoxigenin-linked biotin." Whether/how merely "detecting the released digoxigenin-linked biotin" amounts to "amplifying a signal" is not clear. The step(s) required for "amplifying a signal" appear omitted.



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***Claim Rejections - 35 USC § 102***

Claims 1-2 and 4-6 are rejected under 35 U.S.C. 102(e) as being anticipated by Singh et al. (US 6,770,439).

Singh et al. teach a method for amplifying a signal from a binding assay comprising the steps of:

providing a reaction mixture comprising:

a medium suspected of containing an analyte (see col. 9, lines 16-19, "a large number of proteins in a single sample"),

a first specific binding pair member bound to a support (see col. 9, lines 21-22, "One group of binding proteins is bound to a support"),

a second specific binding pair member bound to a sensitizer (see col. 10, lines 22-28, "Two entities are employed... that bind to the same target moiety. One of the entities generates an active species") capable in its excited state of generating a reactive oxygen species (see col. 11, line 17, "Singlet oxygen"), wherein the proximity of the two specific binding pair members is modulated by the presence of analyte (see col. 39, lines 39-41, "The resulting complex has three components, where the target serves to link the labeled binding members to the support"), and

a substrate bound to the support through a reactive oxygen cleavable linker (see col. 10, lines 24-27, "a susceptible functionality that interacts with the active species resulting in release of the eTag reporter") (see col. 36, lines 32-35, "The solid support may have... e-tag probe covalently or non-covalently bound to the support"),

incubating the reaction mixture (see col. 39, line 51, "mixture is incubated"),

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exciting the sensitizer causing the formation of reactive oxygen (see col. 11, line 17, "Singlet oxygen"), which cleaves the cleavable linker and releases detectable product from the support (see col. 10, lines 24-27, "One of the entities generates an active species. The other entity has a susceptible functionality that interacts with the active species resulting in release of the eTag reporter"),

detecting the released detectable product (see Abstract, "Detection involves the release of identifying tags as a consequence of target recognition"), wherein the step of detecting comprises the steps of:

separating the released detectable product from the substrate bound to the support (see col. 36, lines 19-21, "the subject heterogeneous assays require that the unbound labeled reagent be separable from the bound labeled reagent"),

adding to the separated released detectable product, a third specific binding pair member capable of binding directly to the released detectable product, allowing the third specific binding pair member to bind, and detecting the bound third specific binding pair member (see col. 40, lines 25-41, "e-tags may be reacted with detectable labels" "detectable label may be part of the reagent cleaving the cleavable bond").

With respect to claim 2, Singh et al. teaches a method for amplifying a signal from a binding assay wherein the proximity of the first and second specific binding pair members results from the binding of the first and second specific binding pair members to the analyte (see col. 39, lines 35-41, "sandwich mode", "The resulting complex has three components, where the target serves to link the labeled binding members to the support"), the sensitizer is a photosensitizer (see col. 11, lines 6-7, "squarate derivatives"), the reactive oxygen is singlet oxygen (see col. 11, lines 6-7, "singlet oxygen"), and the excitation step comprises irradiation with light (see col. 10, lines 18-19, "photoactivated excited species").

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With respect to claims 4-6, Singh et al. teaches a method for amplifying a signal from a binding assay wherein the reactive oxygen cleavable linker comprises enamines (see col. 11, line 20), imidazole, oxazole, and thiazole (see col. 12, lines 29-30).

***Claim Rejections - 35 USC § 103***

Claims 3 and 37-43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Singh et al. (US 6,770,439) in view of Oh & Sternberg (US 5,851,778).

Singh et al. teach a method for amplifying a signal from a binding assay as described supra. In addition, Singh et al. teach a method wherein the analyte, first specific binding pair member, and second specific binding pair member are polynucleotides (see Figs. 3A, 3B), the substrate comprises digoxigenin and biotin (see col. 29, lines 6-8, "biotin and strept/avidin... digoxin or derivative thereof and antidigoxin), and detection employs avidin and anti-digoxigenin antibodies (see col. 29, lines 6-8, "biotin and strept/avidin... digoxin or derivative thereof and antidigoxin) bound to a member of a signal producing system.

Singh et al. do not teach a detectable product comprising digoxigenin-linked biotin.

However, Oh & Sternberg teach the use of digoxigenin-linked biotin (see col. 16, lines 30-38, "other tridentates", "digoxin") in energy transfer assays (see col. 17, lines 54+). Therefore, it would have been obvious for a person of ordinary skill in the art to modify the method for amplifying a signal from a binding assay with the use of digoxigenin-linked biotin because Oh & Sternberg discovered that tridentate conjugates do not require "expensive isolation and characterization procedures of prior art reagents" and exhibit "longer shelf life" than prior art counterparts (see col. 18, lines 51-63).

***Response to Arguments***

In prior Office Action, the specification was objected to because, on p. 6, lines 2-4, the mechanism underlying the recited conditional causal relationship was considered indefinite. In addition, on p. 6, lines 4-5, the mechanism underlying the recited conditional causal relationship was considered indefinite. Applicants' argumentation on these matters is fully persuasive and sufficient to overcome these objections. Accordingly, these objections are withdrawn.

In prior Office Action, claims 1-2 and 4-6 were rejected under 35 U.S.C. 102(e) as being anticipated by Singh et al. (US 6,770,439). In response, Applicants argue "[t]here is no disclosure or suggestion in the passages relied on in the Office Action of the addition of a third specific binding pair member capable of binding directly to the released detectable product or of allowing a third specific binding pair member to bind to the released detectable product and detecting the third specific binding pair member" (see Applicants' reply, p. 14, first full paragraph). Applicants then proceed to acknowledge that "Singh states that, where detectable labels are not present on the e-tags, the e-tags may be reacted with detectable labels" (emphasis mine). Applicants' argument is not persuasive in view of Applicants' acknowledgement that "Singh states that, where detectable labels are not present on the e-tags, the e-tags may be reacted with detectable labels" (emphasis mine).

In prior Office Action, claims 3 and 37-46 were rejected under 35 U.S.C. 103(a) as being unpatentable over Singh et al. (US 6,770,439) in view of Oh & Sternberg (US 5,851,778). In response, Applicants amend independent claim 44 to add, *inter alia*, the limitation of a "substrate comprising digoxigenin-linked biotin linked to the substrate through a reactive oxygen cleavable linker" and the steps of releasing and detecting "digoxigenin-linked biotin". With respect to claims 44-46, Applicants' amendment appears sufficient to overcome this rejection. Accordingly, this rejection is withdrawn with respect to claims 44-46.

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With respect to claims 3 and 37-43, Applicants argue that (1) the motivation to combine the teachings of Singh et al. with Oh & Sternberg proffered by the Office Action is not relevant to the presently claimed reagents, and (2) even if motivated, one still would not be in possession of the invention of claims 3 and 37-43, because "[t]here is no recognition of using digoxigenin linked biotin as part of a substrate in an assay where cleavage of an oxidant cleavable linker releases digoxigenin linked biotin as a detectable product" (emphasis mine).

Applicants' arguments are not persuasive. With respect to (1), *supra*, the fact that Applicants recognize a different advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985). With respect to (2), *supra*, Examiner is unable to comprehend Applicants' argumentation premised on the use of indefinite terms (i.e. "substrate", "product") to describe indefinite claim language. Examiner requests further clarification of claim language before engaging in meaningful dialog.

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**Conclusion**

No claims are allowed at this time.

Notwithstanding issues of new matter and indefiniteness, set forth *supra*, claims 44-46 appear free of the prior art.

Applicants' amendment necessitated the new grounds of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Venci whose telephone number is 571-272-2879. The examiner can normally be reached on 08:00 - 16:30 (EST). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

David J Venci  
Examiner  
Art Unit 1641

djv

  
**LONG V. LE** 02/16/06  
**SUPERVISORY PATENT EXAMINER**  
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